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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/632,722	08/04/2000	Michele Himmelspach	235.00	2874

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Baxter Healthcare Corporation
P O Box 15210
Irvine, CA 92614

EXAMINER
ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 08/25/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/632,722	Applicant(s) HIMMELSPACH ET AL.	
	Examiner Hope A. Robinson	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *16, 34-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-15 and 17-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-15 and 17-33) in Paper No. 10 is acknowledged. The traversal is on the ground(s) that claims 35 and 38-43 should also be included in Group I. However, this assertion is not correct as claim 35 is directed to the recombinant production of the protein, which is appropriately placed in Group II, which contains the DNA. Class 435, subclass 69.1 deals with the recombinant DNA technique included in the method of making a protein or polypeptide as set forth in the restriction requirement. The argument that the preparation claims depend from the protein claims is not persuasive as dependency is not a criteria for restriction. Note that claim 16 directed to the DNA depends from claim 1, however, applicant does not offer the same argument to keep the two inventions together. The MPEP sets forth that a restriction requirement is proper if the invention is independent or distinct. Burden of search is another criteria which has been established by the demonstration of a separate status in the art. Thus, the restriction requirement is proper and is final.

Priority

2. It is noted that applicant has claimed priority under 119(a-d) to an Austrian document (A 1377/99), however, the application is missing a certified copy of the document.

Correction is required.

Claim Objections

3. Claims 1 and 17 are objected to because the claim recites Figure I instead of the specific sequence identifier (i.e. SEQ ID NO:). The dependent claims are also included in this objection.

Claim 3 is objected to because the claim recites an extraneous period see item "d) R4 is an amino acid selected from the group Asp. Lys, Thr, or Glu".

Claims 10 and 19 are objected to as being inconsistent as all other dependent claims use lower case when reciting the dependency, however, these claims recite "Claim".

Correction of the above and compliance with the sequence rules is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-15 and 17-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modifications to the sequence via substitution, does not reasonably provide enablement for modifications that involve

deletion of the entire range between Glu226 and Arg 234 or Glu226 and Ile235. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: quantity of experimentation necessary; amount of direction or guidance presented; presence or absence of working examples; nature of the invention; state of the prior art and relative skill of those in the art; predictability or unpredictability of the art and breadth of the claims, each of which is discussed below.

The nature of invention is a factor X analog with a modification in the region of amino acid residues 226-235 with reference to the sequence shown in Figure 1 of the instant application (page 7 of the specification). The specification provides guidance as to what is considered to be a modification. On page 7 it is stated that a modification refers to a mutation, a deletion, an insertion, or a substitution of an amino acid residue within the designated sequence. It is further stated that deletion refers to the absence of at least one of the amino acid residues. However, the guidance/direction provided is inadequate as the specification does not discuss a modification that would result in the deletion of the entire range, however, the claims broadly recite "a modification between Glu226 and Ile235 which encompasses the deletion of the entire range. Further, the definition provided indicates that the entire region can be deleted, since "at least one residue deletion" means that more than one can also be deleted at one time. The

specification does not demonstrate via working examples a Factor X analog with this region deleted, yet such an analog is encompassed by the claimed invention. Therefore, one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims because undue experimentation is required to determine if a factor X analog modified by deletion of the entire range is functional. The prior art does not provide enablement for the missing direction because the prior art enables the modification contemplated in for example claim 3 which involves specific substitutions. As there is no analogous art, no predictability exists. Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1, 2, 8-15 and 17-33 are rejected under 35 U.S.C 102(a) as being anticipated by Himmelspach et al. (WO 98/38317, September 3, 1998) based on the broad recitation of "a modification between Glu226 and Ile235".

Himmelspach et al. teach factor X analogs and the sequence contained in Figure 1 with a 100% sequence identity. Himmelspach et al. also teach modifications to the

sequence. Himmelspach et al. teach a sequence that contains a modification between Glu226 and Ile235 (claim 1) and a modification between Glu226 and Arg234 (claim 2) (see the abstract and pages 8, 9 and 58), as SEQ ID NO: 26 of the reference contain the modification listed for R1-R6 between Glu226 and Ile235 thus, anticipates the claimed invention. In addition, Himmelspach et al. teach that modification in the factor X analog is preferably an exchange of a Factor VIIa/Factor IXa processing site (claim 8, page 7, paragraph 4 of the reference). The reference also teaches that the factor X analogue has a modification in the C-terminal region of the Factor X amino acid sequence (claim 9, see page 11, paragraph 2 of the reference).

Himmelspach et al. teach that there is a modification in the region of the C-terminal beta-peptide cleavage site (claim 10, page 11, third paragraph). The factor X analog is said to contain a modification allowing activation of the factor X analog to Factor Xa, preferably native Factor Xa, *in vivo* (claims 11 and 25, page 13, paragraph 4 of the reference) and *in vitro* activation (claims 12 and 26, page 13, paragraph 3). The factor X analog is said to have an intact beta-peptide (claim 13, page 11, paragraph 3). Factor X is in the form of a double chain molecule (claims 14 and 22, page 15, paragraph 1 of the reference).

Himmelspach et al. teach factor X analogs and a preparation containing factor X analogs (claim 17, see abstract). Himmelspach et al. teach modification located in the C-terminal region of the activation peptide between Gly228 and Arg234 which falls within the range of Glu 226 and Arg234 of claim 18 (see page 7, paragraph 3). It is also taught that the modifications form a cleavage site for factor XIa (claim 19, page 7,

paragraph 4). The modifications contemplated by the reference are identical to the claimed invention, thus a shortened C-terminal is inherent rendering claims 15 and 21 as anticipated. Himmelspach et al. further teach a factor X analog as a single chain molecule (claim 24) which can be present as either Factor X-alpha (claim 20) or with a deletion of the beta- peptide and the preparation contains Factor X analog in enzymatically inactive form and has a purity of at least 80%... and does not contain any inactive, proteolytic intermediates of Factor X/Xa analog (claim 23, page 17, paragraph 3). The preparation taught by the reference is formulated as a pharmaceutical preparation (claim 27, page 19, paragraph 2). It is stated in the reference that the factor X or factor Xa analog is obtained with high stability and structural integrity and is free of inactive Factor X/Xa analog intermediates and autoproteolytic degradation products (claim 28, page 16, paragraph 1). The preparation is described as being bound to a matrix and can be stably stored (claim 29, page 18, paragraph 2 and page 20 paragraph 1). Further, the preparation is said to contain a blood factor (claim 30) as an additional component and the component contains bypass activity (claim 31, page 21, paragraph 4).

Himmelspach et al. teach that the preparation is formulated as a pharmaceutical compound and is present as a multi-component preparation (claim 32, page 22, paragraph 2), said preparation is used to produce a drug/medicament (claim 33, page 22, paragraph 6 and page 23, paragraph 2). Therefore, the teachings of the reference anticipate the claimed invention.

Conclusion

6. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The examiner can normally be reached on Monday-Friday from 9:00 am to 5:30 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S. F. Low, can be reached at (703) 308-2923.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Hope Robinson, MS

Patent Examiner